

Remarks/Arguments:

Reconsideration of this application is respectfully requested. Upon entry of the amendments claims 1-19, 44-49, and 51-52 will be pending. Claims 20-43 were previously canceled without prejudice as directed to non-elected subject matter. Claim 50 was previously canceled, without prejudice or disclaimer, in view of the proposed rule changes by the US PTO to limit the number of claims to 25 total claims.

The specification has been amended herein to correct typographical errors. No new matter has been added.

Claim 1 has been amended so that the claim recites only a single period at the end of the claim. Claim 8 has been amended to more particularly point out the invention. Support for the amendment can be found at least at paragraph [0030] of the application as published. No new matter has been added.

Finally, new claims 51 and 52 have been added herein. Claim 51 recites the invention previously recited by claim 50. Claim 52 recites the portion of claim 8 that has been deleted herein. No new matter has been added.

Specification

The Specification was objected to for containing a typographical error in the Abstract. Applicants have amended the Abstract herein and also corrected a typographical error in the main body of the specification. Accordingly, the objection should be withdrawn.

Claim Objections

Claim 1 was objected to for using a period at each step of the claimed method. The claim has been amended herein as suggested by the Examiner. Accordingly, the objection should be withdrawn.

Rejection under 35 USC § 112

Claim 8 has been rejected under second paragraph as indefinite. According to the Examiner, the ratio of bacteria to bacteriophage is uncertain as the claim is recited. Applicants have amended the claim herein for clarity. The amendment is believed to overcome the rejection. Accordingly, reconsideration and withdrawal of the rejection are requested.

Rejection under 35 USC § 103

Claims 1-19 and 44-49 are rejected as being unpatentable over Swanstorm and Adams ("Swanstorm") in combination with U.S. Patent No. 6,322,783 to Takahashi ("Takahashi"); U.S. Patent Application Publication No. 2004/0091856 to Pelletier et al. ("Pelletier"); and U.S. Patent No. 6,482,632 to Agrawal ("Agrawal").

According to the Examiner, it would have been obvious to one of ordinary skill in the art to modify the methods taught by Swanstorm in order to increase phage yield and purification of the phage through the method claimed in the present invention. *See* Office Action at page 5. The Examiner further asserts that there would have been a reasonable expectation of success, given the knowledge that a two layer agar technique for producing phage has been employed with great success in addition to the application of CsCl purification of phage, taught by Takahashi and Pelletier, and also given the knowledge that reducing a soft layer (semi-solid) to only contain 0.3% agar does not affect phage production, as taught by Agrawal. *See id.*

Applicant respectfully traverses as the rejection is applied to the claims as amended herein. As amended, the claimed invention discloses methods for commercial intermediate to large scale production of bacteriophage stock composition, in which each step is easy to perform and does not require large operating volumes.

As stated by the Examiner (*see* Office Action at page 4), and as described in the instant specification (*see* paragraph [0065] of the published application), the method disclosed by Swanstorm, as well as slightly modified methods, have long been used on a laboratory scale. Particularly, these methods are suitable for the growth and isolation of a specific bacteriophage type or a mutant. Such methods are also used by Takahashi and by Pelletier. However, when multiplication of bacteriophages is required, even at a small laboratory scale, liquid cultures are preferred, as disclosed, for example, by Takahashi (column 17, line 41). Thus, the combination of references teaches away from the claimed invention, which uses a two layer, solid phase/semi-solid phase system.

Up to the time of the present invention, based on the laboratory experience, attempts for scaling up bacteriophage growth were directed toward culture production, which requires the use of very large fermenters that are difficult and expensive to

operate. This is based in part on the fact that the semi-solid layer disclosed by Swanstorm contains agar at a concentration of about 0.7%. Thus, scraping this layer from the bottom layer to enable bacteriophage isolation is not highly efficient. Compare for example 36 ml yield of crude phage extract in Swanstorm (see Swanstorm at page 372, col. 2) with 55 liters of crude phage extract in the present invention (see Fig. 2A of application).

Thus, Swanstorm, neither alone nor in combination with Takahashi and/or Pelletier provide motivation to use a top semi-solid layer with agar concentration of 0.3% for large-scale production of bacteriophage stock composition.

The present invention is based in part on the unexpected finding that reducing the hydrocolloid (e.g. agar) concentration in the top layer not only significantly enhances the efficacy of bacteriophage extraction, but also results in a high bacteriophage titer of at least 10^{11} , typically of 10^{15} to 10^{16} . Such yield increase would not have been obvious to a person skilled in the art at the time of the invention. As it is understood from the context of the disclosure of Agrawal, and as is acknowledged by the Examiner, Agrawal at most suggest that using agar concentration of 0.3% does not affect the phage production. Nowhere in Agrawal is it disclosed or suggested that reducing the top-layer agar concentration would result in an increased bacteriophage titer. Moreover, the reduction in agar concentration could not be interpreted as merely function of up-scaling of the phage production, as it could not be anticipated that the titer will increase. Accordingly, Applicant submits that the combination of references is improper, and that if combined: (i) would render the prior art unsatisfactory for its intended purpose or change the principle of operation of one or more of the references; and/or (ii) would still not achieve the claimed invention with the requisite reasonable expectation of success. See *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976).

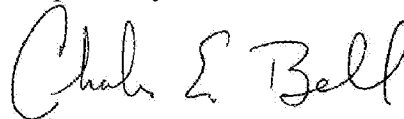
Thus, Applicant respectfully submits that the method of the present invention would not have been obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant submits that this paper is fully responsive. On the basis of the foregoing amendments and remarks, action on the merits of the claims and a Notice of Allowance thereof are respectfully requested. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Without an extension of time, this response is due on or before April 24, 2008. Accordingly, this response is timely filed and no fee is believed due. The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 08-1935, Reference No. 2488.018.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Charles E. Bell". The signature is fluid and cursive, with the first and last names being more prominent.

Dated: April 24, 2008

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